[Billing Code 4140-01-P]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 209 and 37 CFR part 404 to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

FOR FURTHER INFORMATION: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852-3804; telephone: 301-496-7057; fax: 301-402-0220. A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Discovery of Novel PARP Inhibitors that Synergize with Topoisomerase I Inhibitors for Cancer Treatment

Description of Technology: Scientists at the NCI discovered new inhibitors of poly ADP ribose polymerase (PARP). These inhibitors can synergize with topoisomerase I (Top 1) inhibitors, such as camptothecin (CPT), as well as with other cancer therapeutic agents, such as DNA alkylating agents (temozolomide), to enhance the efficacy of current anticancer treatments. The mechanism of action is inhibition of DNA repair mechanism. PARP is a partner of trosyl-DNA phosphodiesterase I (TDP1), a DNA repair enzyme inside the XRCC1 multiprotein-DNA repair complex.

Potential Commercial Applications:

• Used in combination therapy with approved cancer therapeutic agents

• Treatment for BRCA- and homologous repair-deficient cancers

Competitive Advantages: Should boost the efficacy of current anti-cancer treatments

Development Stage: In vitro data available

Inventors: Chrisophe R. Marchand, J. Murai, Yves G. Pommier (all of NCI)

Publications:

1. Maxwell KN, Domchek SM. Cancer treatment according to BRCA1 and BRCA2 mutations. Nat Rev Clin Oncol. 2012 Sep;9(9):520-8. [PMID 22825375]

2. Marchetti C, et al. Olaparib, PARP1 inhibitor in ovarian cancer. Expert Opin Investig Drugs. 2012 Oct;21(10):1575-84. [PMID 22788971]

3. Ellisen LW. PARP inhibitors in cancer therapy: promise, progress and puzzles. Cancer Cell. 2011 Feb 15; 19(2):165-7. [PMID 21316599]

4. Papeo G, et al. Poly(ADP-ribose) polymerase inhibition in cancer therapy: are we close to maturity? Expert Opin Ther Pat. 2009 Oct;19(10):1377-400. [PMID 19743897]

Intellectual Property: HHS Reference No. E-075-2014/0 – Research Tool. Patent protection is not being pursued for this technology.

Related Technology: HHS Reference No. E-199-2010/0 – US Patent Application No. 13/293,282 filed 27 Oct 2011 (allowed)

Licensing Contact: Uri Reichman, Ph.D., MBA; 301-435-4616; ur7a@nih.gov

Deconvolution Software for Modern Fluorescence Microscopy

Description of Technology: This software invention pertains to Joint Richardson-Lucy (RL) deconvolution methods used to combine multiple images of an object into a single image for improving resolution in modern fluorescence microscopy. RL deconvolution merges images with very different point spread functions, such as in multi-view light-sheet microscopes, while preserving the best resolution information present in each image. RL deconvolution is also easily applied to merge high-resolution, high noise images with low-resolution, low noise images, relevant when complementing conventional microscopy with localization microscopy. The technique can be performed on images produced via different simulated illumination patterns, relevant to structured illumination microscopy (SIM) and image scanning microscopy (ISM) resulting in image qualities at least as good as standard inversion algorithms, but follows a simpler protocol

that requires little mathematical insight. RL deconvolution can also be used to merge a series of several images with varying signal and resolution levels. This combination is relevant to gated stimulated-emission depletion (STED) microscopy and shows that high-quality image merges are possible even in cases where no explicit inversion algorithm is known.

Potential Commercial Applications: Microscopy

Competitive Advantages: High image precision for fast moving samples

Development Stage:

• Early-stage

• In vitro data available

Inventors: George H. Patterson, Maria DM Ingaramo, Andrew York, Hari Shroff (all of NIBIB)

Publications:

1. Richardson, William Hadley. Bayesian-Based Iterative Method of Image Restoration. J Opt Soc Am. 1972;62 (1): 55-9. [http://dx.doi.org/10.1364/JOSA.62.000055]

2. Wu Y, et al. Volumetric Isotropic Imaging with Dual-view Plane Illumination Microscopy. Nat Biotechnol., in press.

3. Lucy LB. An iterative technique for the rectification of observed distributions. Astron J. 1974;79(6):745-54. [http://dx.doi.org/10.1086/111605]

Intellectual Property: HHS Reference No. E-038-2014/0 – Software Materials. Patent protection is not being pursued for this technology.

Related Technologies: HHS Reference No. E-005-2012/2 – PCT Application No. PCT/US2013/27413 filed 22 Feb 2013, which published as WO 2013/126762 on 29 Aug 2013 (claiming priority to 23 Feb 2012)

Licensing Contact: Michael Shmilovich, Esq.; 301-435-5019; shmilovm@mail.nih.gov

Collaborative Research Opportunity: The National Institute of Biomedical Imaging and Bioengineering is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize Multifocal High Resolution Microscopy. For collaboration opportunities, please contact Henry Eden, M.D., Ph.D. at edenh@mail.nih.gov or 301-435-1953.

Human Influenza Virus Real-time RT-PCR: Detection and Discrimination of Influenza A (H3N2) Variant from Seasonal Influenza A (H3N2) Viruses, Including H3v and Seasonal H3 Assays

Description of Technology: This invention relates to methods of rapidly detecting influenza, including differentiating between type and subtype. CDC researchers have developed a rapid, accurate, real-time RT-PCR assay that has several advantages over culture and serological tests, which require 5 to 14 days for completion; this assay can also be easily implemented in kit form. To date, hundreds of human cases of infection with the H3N2 variant virus have been confirmed. The increased numbers of human infection of H3N2 variant virus has led to a need for a highly sensitive and specific assay for the diagnosis and confirmation of the H3N2 variant virus.

Potential Commercial Applications:

• Influenza diagnostic using clinical specimens

• High-throughput sample screening

• Government, regional influenza surveillance programs

Competitive Advantages:

• Especially useful for H3N2 screening

• Sensitive detection

• Specific discrimination of influenza subtypes

• Easily formatted as kit or array

• Faster than culturing and serological identification methods

• Less laborious and more objective than immunoassays

Development Stage: In vitro data available

Inventors: Bo Shu, Stephen Lindstrom, Kai-Hui Wu, LaShondra Berman (all of CDC)

Publications:

1. Lindstrom S, et al. Human infections with novel reassortant influenza A(H3N2)v viruses, United States, 2011. Emerg Infect Dis. 2012 May;18(5):834-7. [PMID 22516540]

2. Cox CM, et al. Swine influenza virus A (H3N2) infection in human, Kansas, USA, 2009. Emerg Infect Dis. 2011 Jun;17(6):1143-4. [PMID 21749798]

3. Jhung MA, et al. Outbreak of variant influenza A(H3N2) virus in the United States. Clin Infect Dis. 2013 Dec;57(12):1703-12. [PMID 24065322]

Intellectual Property: HHS Reference No. E-562-2013/0 – US Patent Application No. 61/894,291 filed 22 Oct 2013

Related Technologies:

• HHS Reference No. E-274-2013/0

• HHS Reference No. E-331-2013/0

Licensing Contact: Whitney Blair, J.D., M.P.H.; 301-435-4937; whitney.blair@nih.gov

Improved Methods to Measure Hyaluronan Acid

Description of Technology: The invention is directed to an improved method for measuring the amount of hyaluronan acid (HA) in a biological sample using an ELISA based system. HA is a disaccharide polymer that is expressed at elevated levels in patients afflicted with certain autoimmune diseases, including Graves' ophthalmopathy and rheumatoid arthritis. The amount and the length of HA present in a patient sample varies.

When compared to existing assays, the invention assay provides a more accurate and sensitive way to measure HA. Specifically, the first step in the invention assay involves determining the size range of the average molecular weight of HA in the sample. Next, the amount of HA in the sample is quantified using an ELISA system wherein HA binds to hyaluronan binding protein (HABP). Then, the binding results are compared against a control sample containing HA at an average molecular weight similar to that of HA in the sample being tested. Thus, the invention assay takes into account two variables that lead to significant errors in calculating the concentration of HA in a biological sample: (1) The wide range of HA particle sizes in a sample, and (2) differing binding efficiencies between HABP and HA at different particle sizes.

Potential Commercial Applications:

• Diagnostic Test

• Personalized Medicine

Competitive Advantages: More accurate and sensitive quantification of HA in biological samples when compared to commercially available ELISA kits.

Development Stage:

• Early-stage

• In vitro data available

• Prototype

Inventors: Marvin C. Gershengorn and Christine C. Krieger (NIDDK)

Publication: Krieger CC, Gershengorn MC. A modified ELISA accurately measures secretion of high molecular weight hyaluronan (HA) by Graves' disease orbital cells. Endocrinology. 2014 Feb;155(2):627-34. [PMID 24302624]

Intellectual Property: HHS Reference No. E-538-2013/0-US-01 – US Application No. 61/860,722 filed 31 Jul 2013

Licensing Contact: Lauren Nguyen-Antczak, Ph.D., J.D.; 301-435-4074; lauren.nguyen-antczak@nih.gov

Human iPSC-Derived Mesodermal Precursor Cells and Differentiated Cells

Description of Technology: Cells, cell culture methods, and cell culture media compositions useful for producing and maintaining iPSC-derived cell lines that are of higher purity and maintain cell type integrity better than current iPSC-derived cell lines are disclosed. Human induced pluripotent stem cells (hiPSCs) can be generated by

reprogramming somatic cells by the expression of four transcription factors. The hiPSCs exhibit similar properties to human embryonic stem cells, including the ability to self-renew and differentiate into all three embryonic germ layers: ectoderm, endoderm, or mesoderm. Human iPSCs can be induced into any cell type and, since they can be maintained over many passages, they can serve as an almost unlimited source to generate cells from any given person. These properties make iPSC-derived cells a valuable product for cell therapies and toxicology or pharmaceutical high throughput screens. NIH investigators disclose an iPSC-derived mesodermal precursor cell line, positive for CD34 and CD31 expression, that may be used to produce at least four different cell types. When cultured under appropriate conditions, these mesodermal precursor cells can be used to produce hematopoietic stem cells, mesenchymal stem cells, smooth muscle cells, or unlimited functional endothelial cells.

Potential Commercial Applications:

• The iPSC-derived mesodermal precursor cell (MPC) line described here can be used to produce hematopoietic stem cells, mesenchymal stem cells , smooth muscle cells, or unlimited functional endothelial cells.

• The differentiated cells produced using the disclosed methods and MPC can be used for screening, as well as therapeutic applications.

Competitive Advantages: The mesodermal precursor cells have the ability to maintain their phenotype for extended periods without differentiating, when maintained under appropriate conditions.

Development Stage:

• Early-stage

• In vitro data available

• In vivo data available (animal)

Inventors: Drs. Manfred Boehm (NHLBI), Guibin Chen (NHLBI), Mahendra Rao (NIAMS), and André Larochelle (NHLBI)

Intellectual Property: HHS Reference No. E-342-2013/0 – US Provisional Application No. 61/885,209 filed 01 Oct 2013

Related Technologies:

• HHS Reference No. E-762-2013/0 – US Provisional Application No. 61/904,999 filed 15 Nov 2013

• HHS Reference No. E-763-2013/0 – US Provisional Application No. 61/905,002 filed 15 Nov 2013

Licensing Contact: Sury Vepa, Ph.D., J.D.; 301-435-5020; vepas@mail.nih.gov

Collaborative Research Opportunity: The National Heart, Lung, and Blood Institute is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate or commercialize this technology. For collaboration opportunities, please contact Denise Crooks at crooksd@nhlbi.nih.gov.

Silica Exposure Safety: Mini-Baghouse Systems and Methods for Controlling Particulate Release from Large Sand Transfer Equipment

Description of Technology: CDC scientists have developed an effective control for release of silica-containing dusts by using retrofitted mini baghouses for thief hatches on sand transfer trucks. Retrofit of the mini baghouses on sand transfer trucks will

significantly reduce silica dust release and silica exposures in the workplace and surrounding community.

In the U.S., virtually every new oil and gas well is hydraulically fractured (HF) to stimulate well production. Each HF operation has 2-4 sand transfer trucks in use, and tens of thousands of pounds of sand are used for each stage of each multi-stage fracturing. Currently, there are no truck-mounted engineering controls for silica release at HF operations, posing an elevated risk of silica exposure to personnel and surrounding areas. CDC results have shown that silica workplace exposures at HF sites are completely uncontrolled at present (with the exception of personal respirator use), and silica exposures are likely to be the most significant and hazardous occupational chemical exposure on HF sites. Additionally, CDC field research has shown that personal breathing zone silica concentrations regularly exceed the maximum use concentration for both half-mask and full-face air purifying respirators. Use of this mini baghouse technology (multiple mini baghouse retrofits to sand trucks) will serve to limit release of silica dust, thereby diminishing silica exposure and increasing safety.

Potential Commercial Applications:

• Controlling occupational exposure to silica, especially for work involving sand transfer trucks

• Retrofitting currently operating heavy equipment

• Gas and oil well-workers' well-being concern groups

• Hydraulic fracturing operations situated near populated areas and associated insurers

• Occupationally-mandated pneumoconiosis, and/or silicosis prevention programs for complying with safety regulations

Competitive Advantages:

• Designed for retrofitting "thief hatches" of existing machinery

• This technology will reduce silica exposure near hydraulic fracturing sites, helping to diminish one of the most hazardous exposure risks of such operations

• Provides previously unavailable truck mounted engineering controls for silica release at hydraulic fracturing operations

Development Stage:

• In situ data available (on-site)

• Prototype

Inventors: Eric J. Esswein, Michael Breitenstein, John E. Snawder, Michael G. Gressel, Jerry L. Kratzer (all of CDC)

Intellectual Property: HHS Reference No. E-291-2013/0 – US Application No. 13/802,265 filed 13 Mar 2013

Related Technologies:

• HHS Reference No. E-312-2013/0

• HHS Reference No. E-498-2013/0

Licensing Contact: Whitney Blair, J.D., M.P.H.; 301-435-4937; whitney.blair@nih.gov

Dengue Vaccines: Tools for Redirecting the Immune Response for Safe, Efficacious Dengue Vaccination

Description of Technology: This CDC-developed invention relates to dengue vaccines that have been specifically developed for improved efficacy and directed immune response to avoid antibody-dependent enhancement (ADE) safety issues that, theoretically, may be associated with dengue vaccines and vaccinations. Dengue viral infection typically causes a debilitating but non-lethal illness in hosts. However, dengue hemorrhagic fever (DHF), the much more severe and life-threatening condition, is generally attributed to secondary dengue infections caused by a serotype different from the initial infection serotype by way of ADE. This effect, particularly notable in dengue viruses, should be given special consideration during vaccine design and construction.

This *in vivo*-validated technology provides a strategy and mechanism for increasing the safety of dengue vaccines and diminishing the likelihood of such vaccines inadvertently harming a recipient due to ADE-mediated effects. Any safe, effective dengue vaccine must produce well-balanced and tetravalent (for all four dengue serotypes) protective immunity. Despite decades of investigative effort there remains no effective, commercially available dengue vaccine and the greatest hurdle has been the difficulty of rapidly inducing this balanced immunity to all four dengue serotypes.

With this invention, CDC researchers have developed a cross-reactivity reduced dengue serotype 1 (DENV-1) DNA vaccine engineered to directly address ADE-related vaccine safety concerns. *In vivo* murine testing of wild-type and cross-reactivity-reduced vaccines demonstrated that this theoretical vaccine safety concern is real and that the cross-reactivity reduced DNA vaccine dramatically reduces dengue vaccination safety risk while increasing protective antibody responses. Properly developed and

implemented, this novel vaccination strategy should help overcome this previously-unaddressed hindrance to dengue vaccine development.

Potential Commercial Applications:

• Creation of a safe, efficacious and well-balanced dengue virus vaccine

• Improving currently developed/developing dengue vaccines to mitigate potential antibody-dependent enhancement safety issues

• Research tools for vaccine development programs for other flaviviruses, HIV

Competitive Advantages:

• Murine in vivo studies indicating proof-of-principle, safety and efficacy

• Addresses a long-standing “serotype immunity balancing” issue for dengue vaccine development

• Presently there are no safe, effective commercially available dengue vaccines

Development Stage:

• In vitro data available

• In vivo data available (animal)

Inventors: Gwong-Jen Chang, Wayne Crill, Holly Hughes, Brent Davis (all of CDC)

Publication: Crill WD, et al. Sculpting humoral immunity through dengue vaccination to enhance protective immunity. Front Immunol. 2012 Nov 8;3:334. [PMID 23162552]

Intellectual Property: HHS Reference No. E-289-2013/0 -

• US Application No. 61/549,348 filed 20 Oct 2011

• PCT Application No. PCT/US2013/060872 filed 18 Oct 2012

Licensing Contact: Whitney Blair, J.D., M.P.H.; 301-435-4937; whitney.blair@nih.gov

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